REMARKS

The Official Action dated November 20, 2006 has been carefully considered. Accordingly, it is believed that the present Amendment places this application in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, claim 14 is amended to include a limitation from claim 15 and to clarify the claimed method and claim 15 is cancelled. Claim 16 is amended to change its dependency from cancelled claim 15 to claim 14, claim 18 is amended to recite IgG in accordance with the teachings in the specification in the paragraph bridging pages 3 and 4, and claims 18 and 19 are amended to correspond with claim 17. Finally, withdrawn claims 22 and 23 are amended to clarify the methods therein, in accordance with the teachings of the specification, for example at pages 12-13. It is believed that these changes do not involve any introduction of new matter, whereby entry is believed to be in order and is respectfully requested.

In the Official Action, the Examiner made the restriction requirement under 35 U.S.C. §121 final and therefore withdrew claims 20-23 as being directed to a nonelected invention. As claim 14 has been identified as a linking claim, Applicants request rejoinder of withdrawn claims 20-23 upon the allowance of linking claim 14.

Claims 14 and 19 were objected to on the basis that claim 14 employed an undefined abbreviation (ABPA) and claim 19 was a duplicate of claim 18. These objections are traversed with respect to the present claims. Particularly, claim 14 recites allergic bronchopulmonary aspergillosis (ABPA), and claim 19 specifies that the level of antibodies of the IgE class is determined while claim 18 recites that the level of antibodies of the IgE class or IgG class is determined. It is therefore believed that the objections have been overcome. Reconsideration is respectfully requested.

Claims 14-19 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In claim 14, the Examiner questioned if it is the antibody or the allergen that comprises the capacity to "discriminate with 100% specificity" and questioned the significance of such. The Examiner noted that claim 18 recited IgE twice, and with respect to both claims 18 and 19, questioned how antibodies are determined.

This rejection is traversed and reconsideration is respectfully requested. More particularly, claim 14 recites that the one or more ABPA-related recombinant allergens discriminate with 100% specificity between ABPA and allergic sensitization to *A. fumigatus*. As explained in the present specification, Applicants' discovery that some allergens from *A. fumigatus* only bind to antibodies from ABPA patients, but not to antibodies from non-ABPA patients, allows the use of the present methods to discriminate between ABPA patients and non-ABPA patients. As noted in the present specification, for example beginning at page 1, line 22, ABPA is an immune disease that ranges from asthma to fatal destructive lung disease and, because of its severity, ABPA should, at an early stage, be ruled out in patients with chronic asthma or cystic fibrosis. Thus, the discovery of allergens which discriminate with 100% specificity between ABPA and allergic sensitization to *A. fumigatus* provides for the important diagnostic methods of the present invention.

Present claim 18 recites that the level of antibodies of the IgE class or IgG class or subclasses thereof is determined, and the duplicate recitation of IgE has been omitted. Additionally, claims 18 and 19 recite that the level of antibodies is determined, in accordance with the method recited in claim 17.

It is therefore submitted that claims 14-19 are definite to one of ordinary skill in the art in accordance with the requirements of 35 U.S.C. §112, second paragraph, whereby the rejection has been overcome. Reconsideration is respectfully requested.

Claims 14-19 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Claims 14-19 were also rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner asserted that the breadth of Applicants' claims is not limited to the two allergens Asp f4 and f6 employed in the working examples, but encompasses the use of any ABPA-related recombinant allergen although the specification does not disclose any epitopes of *A. fumigatus* allergens that are bound by antibodies from ABPA patients but not *A. fumigatus* allergy patients, and the specification does not appear to teach what structure or structures are required of molecules recognized only in ABPA patients. The Examiner also asserted that the specification discloses that 100% specificity can be obtained by use of a recombinant Asp f4 and f6 but does not indicate any other allergens which may be used in methods that discriminate between two patient populations with 100% specificity.

This rejection is traversed and reconsideration is respectfully requested. That is, as defined by claim 14, the present invention is directed to a method for the diagnosis of ABPA in a human individual. The present invention is based on Applicants' discovery that there are allergens from *A. fumigatus* that only bind to antibodies from ABPA patients and do not bind to antibodies from non-ABPA patients. Claim 14 therefore appropriately recites that the diagnostic method comprises determining if the individual carries antibodies reactive with one or more ABPA-related recombinant allergens, which allergens are derived from *A. fumigatus* and discriminate with 100% specificity between ABPA and allergic sensitization to *A. fumigatus*. The present specification both describes this invention and enables one of ordinary skill in the art to perform the invention.

As noted by the Examiner, the present specification exemplifies two of such allergens. Moreover, the present specification provides detailed descriptions of techniques for cloning

of allergens from *A. fumigatus* (pages 4-7) and the determination of the ability of such allergens to discriminate with 100% specificity between ABPA and allergic sensitization to *A. fumigatus* is clearly within the level of one of ordinary skill in the art, particularly in view of the detailed methods described at pages 11-20 of the present specification. Accordingly, one of ordinary skill in the art can practice the presently claimed methods without undue experimentation and Applicants' failure to disclose each and every allergen which may be used in the present methods does not mean that the present claims and specification do not comply with the written description requirement or do not enable the claimed methods under 35 U.S.C. §112, first paragraph.

Further, one of ordinary skill in the art, following the procedures and techniques described in detail in the present specification, can easily determine if an allergen derived from *A. fumigatus* discriminates with 100% specificity between ABPA and allergic sensitization to *A. fumigatus*. In this regard, the present specification indicates that not all allergens derived from *A. fumigatus* exhibit such specificity, and the present methods employ only that subset of allergens derived from *A. fumigatus* which in fact exhibit such specificity. Again, while Applicants do not describe by sequence each and every allergen which exhibits such specificity, one skilled in the art, using the procedures and techniques described in the present specification, can make such a determination without undue experimentation.

As matter of Patent Office practice, a specification disclosure which contains the teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of §112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support, *In re Marzocchi*, 169 U.S.P.Q. 367, 369

(C.C.P.A. 1971) (emphasis by court). In any event, it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement, *Id.* at 370 (emphasis by court). The Official Action fails to provide any evidence or reasoning which is inconsistent with the statements set forth in the present specification relied upon for the enabling disclosure. Accordingly, Applicants are entitled to claim a method as set forth in claim 14, based on their discovery that there are allergens from *A. fumigatus* that only bind to antibodies from ABPA patients and do not bind to antibodies from non-ABPA patients, with 100% specificity.

It is therefore submitted that the specification provides a written description of and enables the claimed methods whereby the rejections under 35 U.S.C. §112, first paragraph, have been overcome. Reconsideration is respectfully requested.

Claims 14-19 were also rejected under 35 U.S.C. §103(a) as being unpatentable over the Borga Ph.D. dissertation from the Karolinska Institute, 1990, in view of Moser et al, *The Journal of Allergy and Clinical Immunology*, 93 (1(1)):1-11 (1994). The Examiner asserted that Borga teaches methods of detecting IgE antibodies that bind *A. fumigatus* allergens using in vitro immunoassays and identified 8 allergens that were only recognized by ABPA patients and 4 allergens which were only recognized in *A. fumigatus* allergy patients. The Examiner asserted that Borga further teaches that such differences are of diagnostic value, referring to the present specification at pages 17-18 and that the allergens of Borga discriminate with 100% specificity. The Examiner relied on Moser et al as teaching the use of recombinant allergens and the Examiner concluded it would have been obvious to perform the diagnostic method taught by Borga using recombinant allergens. Finally, the Examiner requested that

Applicants submit a complete copy of Borga as the Examiner was only able to locate the Abstract.

This rejection is traversed and reconsideration is respectfully requested. Applicants submit that the claimed methods for the diagnosis of ABPA in a human individual are not obvious over Borga in view of Moser et al.

Initially, in accordance with the Examiner's request, submitted herewith is a complete copy of Borga "*Allergens of Aspergillus Fumigatus, Immunochemical Characterization and Purification of Allergens Important in Allergic Disease,*" Department of Clinical Immunology at Karolinska Hospital, Karolinska Institute, Stockholm, Sweden (1990), and publications I-V cited at page 4 of Borga, on which the Borga thesis is based. The Borga thesis and publications I-V are listed on the attached Form PTO-1449 so that the Examiner may make them of record in their entirety in the application. As these publications are submitted at the Examiner's request, it is not believed that any fee is required in connection with this submission. However, in the event that the Examiner determines that a fee under 37 C.F.R. 1.97 is required, please charge any such fee to Deposit Account No. 04-1133.

As noted above, the present invention is based on Applicants' discovery that there are some allergens from *A. fumigatus* that only bind to antibodies from ABPA patients, but not to antibodies from non-ABPA patients, thereby allowing for diagnosis between ABPA patients and non-ABPA patients. Prior to the present invention, it was very difficult to distinguish, particularly at an early stage, a patient suffering from ABPA from a patient suffering from allergic hypersensitivity. However, owing to the severity of ABPA, it is advantageous to determine ABPA diagnosis at an early stage, particularly, for example, in patients with chronic asthma or cystic fibrosis. Thus, the presently claimed diagnostic methods provide an important advance in the art.

Borga discloses a study of allergens of *A. fumigatus*. At pages 14-15, Borga discloses that *A. fumigatus* causes a number of diseases mainly located in the lung or airways and describes a number of specific diseases including, among others, ABPA. At page 21, Borga discloses that the aims of the study were to evaluate the usefulness of certain techniques in the study of mold allergens, with specific reference to *A. fumigatus*, to study the strain, batch and source material variability of *A. fumigatus*, and to characterize IgE-binding components in *A. fumigatus*, studying sera from atopic allergy and ABPA patients, and to purify and further characterize a dominating allergen. At page 42, Borga discloses that 35 different IgE binding components were detected analyzing sera from the atopic allergy patients and 39 binding components were detected analyzing the ABPA sera, wherein 31 of these components were common to both groups while 4 intermediate components were detected only by sera from the atopic allergy patients and 8 minor or intermediate components were detected only by sera from ABPA patients. Figs. 10a and 10b at pages 43 and 44 of Borga illustrate strong, moderate and weak bands, but Applicants find no teaching by Borga as to the criteria for these categories or the criteria for no indicated bands and particularly whether no bands are actually 0.0% binding or binding below a certain threshold level. Thus, the teaching of Borga that a component "only" binds to sera from ABPA patients is not equivalent to a teaching of the present claim limitation of an allergen which discriminates with 100% specificity between ABPA and allergic sensitization.

As noted, Borga teaches that 31 components react with both types of sera, leading to the conclusion that "considerable similarities were seen between the atopic allergy group and the ABPA group" (page 42, lines 20-24 and reference IV, page 8, lines 21-26). Further, while Borga identifies 4 major components of molecular weight, 90, 50, 20 and 19 kD, respectively, these major components are present in both types of sera (page 42, lines 25-30

and Figs. 10a and 10b). Although Borga states that both major components and group-specific components could be of potential diagnostic value, Borga does not disclose how this diagnostic value could be turned into a diagnostic method, and particularly does not teach or suggest that ABPA could be distinguished from allergic sensitization to *A. fumigatus*. Accordingly, while Borga provides detailed information of *A. fumigatus*, Borga importantly provides no teaching or suggestion of any method for discriminating between ABPA and allergic sensitization, particularly with 100% specificity, as presently claimed.

The Examiner asserted in the Official Action that the present specification at page 17, line 36-page 18, line 15 teaches the diagnostic value of Borga's identification of 8 allergens that were only recognized by ABPA patients and 4 allergens which were only recognized by *A. fumigatus* allergy patients. However, the reference at pages 17 and 18 in the present specification to Borga's teachings does not indicate that the individual allergens discriminate with 100% specificity between ABPA and allergic sensitization to *A. fumigatus*. In fact, the present specification at page 18, lines 16-28 indicates that further testing should be performed in order to identify and isolate allergens suitable for use in the present methods. Thus, the present specification recognizes the deficiencies in the teachings of Borga with respect to methods as presently claimed.

In order to render a claimed invention obvious, the prior art must enable one skilled in the art to make and use the claimed invention, *Motorola, Inc. v. InterDigital Tech Corp.*, 43 U.S.P.Q. 2d 1481, 1489 (Fed. Cir. 1997). In view of the failure of Borga to teach any allergen which discriminates with 100% specificity between ABPA and allergic sensitization to *A. fumigatus*, or to even recognize that such discrimination is possible, Borga fails to enable one of ordinary skill in the art to make and use the presently claimed methods for diagnosis of ABPA in a human individual. Moser et al's disclosure of recombinant *A.*

fumigatus does not resolve this deficiency. Accordingly, the combination of Borga and Moser et al does not render the presently claimed invention obvious under 35 U.S.C. §103.

It is therefore submitted that the methods defined by claims 14-19 are nonobvious over and patentably distinguishable from Borga in view of Moser et al, whereby the rejection under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

Finally, claims 14-19 were rejected on the ground of nonstatutory obviousness-double patenting as being unpatentable over claims 1-4, 7, 8 and 12-16 of U.S. Patent No. 6,830,891. This rejection is traversed. However, to expedite prosecution, a Terminal Disclaimer is submitted herewith. The Terminal Disclaimer simply serves the statutory function of removing the rejection of double patenting and raises neither presumption or estoppel on the merits of the rejection, *Quad Environmental Technologies v. Union Sanitary District*, 20 U.S.P.Q. 2d 1392 (Fed. Cir. 1991). Thus, the rejection on the ground of nonstatutory obviousness-double patenting has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the objections and rejections set forth in the Official Action, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,

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